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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Jeffrey Kitzler

RM.NDJ

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EXAMINER

KASTEN, ROBERT J

ART UNIT

PAPER NUMBER

4191

MAIL DATE

DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/532,403	Applicant(s) KITZLER ET AL.	
	Examiner ROBERT KASTEN	Art Unit 4191	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 October 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 22 April 2005 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

1053DETAILED ACTION

1. This is the first, non-final action on the merits.
2. Claims 1-20 are pending herein.

Objections

3. Claim 20 objected to because of the following informalities: addition of CAS # redundant due to the presence of both the commercial dye name (Nile Red), as well as the chemical formula. Appropriate correction is required.

Drawings

4. The drawings are objected to because they fail to support the description put forth in specification, namely that "bands containing as little as 10 ng protein can be seen in **FIG. 1**". Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or

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"New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-3, 8-9, 17 are rejected under 35 U.S.C. 102(b) as being anticipated by GUTTMAN et. al (*Journal of Chromatography A*, 894 (2000) pgs. 329-335), from hereon in referred to as GUTTMAN.

a. GUTTMAN teaches a method and subsequent results for a process of analyzing covalently and non-covalently labeled proteins using sodium dodecylsulfate gel electrophoresis, the gel being a composition of agarose and polyacrylamide, from hereon in referred to as SDS-PAGE. In the method described herein, samples of protein are prepared to a final composition of ".5 mg/ml in 50 mM Tris, 50 mM TAPS, .05% SDS and 10% sucrose-containing buffer, and boiled in a water bath for 5 min after the addition of 2.5% 2-mercaptoethanol....and were labeled by complexation with the fluorescence staining dye Sypro Red...(page 331, para. 3)" The gel used was an agarose gel

with "linear polyacrylamide...added to the melted agarose in 2% final concentration (page 332, para 1)." GUTTMAN also discloses multiple runs (pg 332, para 1), which the examiner has construed to mean the SDS-PAGE gels were subjected to a standard electrophoresis protocol, such as application of some electric field, in order to separate the protein samples

b. Concerning Claim 1, GUTTMAN proposes a method that sample mixture dispersed in buffer (sample added to Tris and TAPS), with detergent added such that it anticipates the required <.1% claimed herein (.05% SDS), for the purpose of running gel electrophoresis on the sample (an SDS-PAGE gel). Finally, the sample mixtures of GUTTMAN include the fluorescent dye Sypro Red.

c. Concerning Claim 2, GUTTMAN's method uses SDS-PAGE for the protein separation (page 332, para 1).

d. Concerning Claim 3, GUTTMAN uses SDS as the detergent (page 331, para. 3)"

e. Concerning Claims 8-9, and 17 GUTTMAN teaches a running buffer with SDS at a concentration of .05% (page 331, para. 3)".

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 4-6, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over GUTTMAN in view of Sigma Aldrich .

a. Concerning Claims 4-6, GUTTMAN discloses the staining of an SDS-PAGE gel with Sypro Red, a fluorescent dye, for the purpose of subsequent imaging and sample quantification/qualification.

i. GUTTMAN does not teach the use of the fluorescent dyes described in the claimed invention.

ii. However, the claimed dyes, Nile Red and Phosphine dyes, are both commercially available dyes and may be purchased online at websites, www.sigmaaldrich.com.

iii. At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to use any other fluorescent dye commercially available on the market because, with a finite amount of commercially available fluorescent dyes formulated for specific uses depending on the sample to be stained, the choice of one dye over another is not a patentable choice, especially in the claimed case, where the claimed invention does not suggest that the use of these known dyes would yield unexpected results. The "obvious to try" rationale stipulates that "choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success" does not pass the non-obvious test required for a claimed invention (MPEP 2141, part III.)

11. Claims 7, 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over GUTTMAN in light of LAEMMLI et al (*Nature Vol. 227 (1970), pgs. 680-685*), from here on in referred to as LAEMMLI, and CANNON-CARLSON et al, from here on in referred to as CANNON-CARLSON (*An. Bio. 246, 146-148 (1997)*).

a. Concerning all 3 claims, GUTTMAN discloses an SDS-PAGE gel electrophoresis method with the use of a buffer solution with components Tris and TAPS, both at 50 mM, at a pH of 8.4, as well as with a detergent, SDS, at a concentration of .05%.

- i. GUTTMAN does not expressly teach the limitations in buffer composition as claimed, namely the buffer composition of claims 7 and 18.
- ii. However LAEMMLI discloses a buffer recipe identical to the claimed buffer (pg 681, para 5).
- iii. At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to combine the buffer composition of LAEMMLI with the method of GUTTMAN since the LAEMMLI buffer composition is an established and often copied composition, especially useful for the electrophoresis of protein samples. The ubiquitousness of the buffer composition is evident from the article by CANNON-CARLSON which discloses "The Laemmli SDS-PAGE method is among the most commonly utilized analytical techniques in protein biochemistry (para 1)."

12. Claims 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over GUTTMAN in light of FRAAIJE et al (*Applied and Environmental Microbiology*, FEB. 1997, pgs 435-439), from here on in referred to as FRAAIJE.

- a. Concerning both claims, GUTTMAN discloses an SDS-PAGE gel electrophoresis method with all of the limitations of Claim 1 (see rejection above).
 - i. GUTTMAN does not expressly disclose a step for visualizing the separated proteins.
 - ii. However, FRAAIJE discloses a method in which an SDS-PAGE procedure is followed with a visualization by UV illumination of a flavin labeled vanillyl-alcohol oxidase (pg 436, para 1).

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iii. At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to take the fluorescently stained sample of GUTTMAN and photograph it while being illuminated by UV light as in FRAAIJE as this is a well established method to determine the success of an analytical experiment such as an SDS-PAGE gel.

13. Claims 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over GUTTMAN in light of FRAAIJE as applied to claims 10-11 above and further in view of MIRZA et al (*American Society for Mass Spectrometry, 2000, 11, 356-361*), from here on in referred to as MIRZA.

a. Concerning both claims 12 and 13, GUTTMAN discloses all of the limitations of claim 1 (see rejection above). FRAAIJE discloses an obvious analytical step in many SDS-PAGE experiments.

i. Neither of them expressly disclose a destaining of the gel.

ii. However, MIRZA discloses an SDS-PAGE method where the gel is washed multiple times with water (pg 357).

iii. At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to wash the stained gel of modified GUTTMAN with water after electrophoresis to wash the excess dye off of the gel sample to eliminate background noise for the UV illumination step, which has already been found to be an obvious extension of the dependent claim.

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14. Claims 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over GUTTMAN in light of FRAAIJE and MIRZA as applied to 12-13, and further in light of AMERSHAM BIOSCIENCES (*Application Note 63-0031-04*), from here on in referred to as AMERSHAM.

a. Concerning Claim 14, modified GUTTMAN discloses all of the limitations of claim 12 (see rejection above).

i. None of the references expressly disclose a destaining of the gel with the claimed solution.

ii. However, AMERSHAM suggests that with the use of their fluorescent stain products, there is a destaining step associated with all of them. For Sypro Tangerine, the suggested destaining method is to wash “for 30 min in 50 ml of PBS buffer (pg 2, protocol 3).” According to page 1 of the same document, AMERSHAM's PBS recipe contains 2.7 mM potassium chloride (KCl).

iii. At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to use the PBS wash of AMERSHAM in the sustaining step of modified GUTTMAN. A PBS wash is necessary to destain some fluorescent dyes and has been proven successful.

15. Claims 15-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over GUTTMAN in light of LEE et al (*Journal of Virological Methods* 84 (2000) 77-89), from here on in referred to as LEE.

a. Concerning both claims, GUTTMAN teaches all the limitations of claim 1 (see rejection above).

i. GUTTMAN does not expressly teach that the proteins are recovered for future processing, purification, or analysis.

ii. However, LEE discloses the use of a Western Blot assay after an SDS-PAGE experiment on prion protein (pg 79, para 4).

iii. At the time of the invention, it would have been *prima facie* obvious to one of ordinary skill in the art to supplement the SDS-PAGE method of GUTTMAN with the Western Blot of LEE. Western Blotting is a common technique used for protein analysis that involves the removal of protein from an analytical gel onto a nitrocellulose membrane where they can be washed with solutions of various antibodies, such as fluorescently labeled antibodies, which can selectively tag proteins separated by the gel for further analysis. This technique is well known to one of ordinary skill in the art and is described LEE (pg 79, column 2, para 2).

Conclusion

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT KASTEN whose telephone number is (571)270-7598. The examiner can normally be reached on Mon-Thurs, 8am to 5pm EST.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Barbara Gilliam can be reached on 571-272-1330. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ROBERT KASTEN/
Examiner, Art Unit 4191

/Barbara L. Gilliam/
Supervisory Patent Examiner, Art Unit 4191